REMARKS

Applicants thank the Examiner for his generous time and for his review of the instant application. For the reasons stated below, the rejections of the presently pending claims are respectfully traversed. Claims 1-5 are presented for examination.

Rejection Under 35 U.S.C. §101

The Examiner has maintained the rejection of Claims 1-5 under 35 U.S.C. § 101 as lacking a specific and substantial utility. The Examiner continues to argue that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. In particular, the Examiner argues that because there is no utility for the polypeptide of SEQ ID NO:64, there is no utility for the claimed antibodies that specifically bind to that polypeptide.

For the reasons of record and the additional reasons discussed below, Applicants respectfully disagree with this rejection because there is a utility for both the polypeptide of SEQ ID NO:64 and the antibodies that bind to that polypeptide.

The Examiner acknowledges that he has previously examined the PRO3566 nucleic acid sequences, found a substantial utility for those claimed sequences, and approved them to issue as a patent. However, the Examiner argues that the data in Example 18 that are based upon quantitative RT-PCR results do not demonstrate utility for the PRO3566 polypeptide, or the claimed antibodies that bind to the PRO3566 polypeptide. Specifically, the Examiner argues that there is no utility for the claimed antibodies since Applicants allegedly have not demonstrated that the PRO3566 polypeptide level is appreciably different in cancer. In support of his position, the Examiner indicates that larger differences in nucleic acid levels would be required to render the claimed invention as having utility without resorting to undue further research experimentation. The Examiner continues to argue that as a general rule mRNA levels are not predictive of protein levels. The Examiner discounts the various declarations (e.g., Grimaldi, Polakis I, Polakis II, and Scott) and the scientific literature that have been submitted by Applicants rebutting the Examiner's utility arguments.

The Examiner goes on to argue that:

> the instant application has only disclosed that the PRO3566 polynucleotide is differentially expressed in melanoma and esophageal tumor. The specification does

> not indicate that the PRO3566 polypeptide has been differentially expressed in the melanoma and esophageal tumor sample tested. Given the asserted increase in PRO3566 expression, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that an increase in mRNA expression would correlate with significantly increased polypeptide levels. Further research needs to be done to determine whether the purported increase in PRO3566 DNA supports a role for the peptide in cancerous tissue; such a role has not be suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. ... Accordingly the specification's assertions that the PRO3566 proteins have utility in the fields of cancer diagnostics is not substantial.

Office Action at 18-19.

Applicants incorporate by reference their previously submitted arguments, and for the reasons of record assert that the specification contains a disclosure of utility and therefore must be taken as sufficient to satisfy the utility requirement of 35 U.S.C. § 101. Applicants also submit that for reasons of record, the Examiner has not met his burden of providing evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility. However, even if the Examiner has met his initial burden, Applicants' previously submitted rebuttal evidence and additional evidence submitted herewith is sufficient to prove that it is **more likely than not** that a person of skill in the art would be convinced, **to a reasonable probability,** that the asserted utility is true. As stated previously, Applicants' evidence need not be direct evidence, so long as there is a reasonable correlation between the evidence and the asserted utility. **The standard is not absolute certainty.**

Substantial Utility

Summary of Applicants' Arguments and the Examiner's Response

Applicants remind the Examiner that the asserted utility rests on the following argument:

1. Applicants have provided reliable evidence that mRNA for the PRO3566 polypeptide is expressed at least two-fold higher in normal skin and esophageal tumor tissue as compared to melanoma and normal esophageal tissue, respectively;

2. Applicants assert that it is well-established in the art that differential levels of mRNA for a particular protein, *e.g.* decreased levels, generally leads to corresponding differential levels of the encoded protein, *e.g.* decreased levels; and

3. Given the differential expression of the PRO3566 mRNA in melanoma and esophageal tumors as compared to their normal tissue counterparts, it is more likely than not that the PRO3566 polypeptide is also differentially expressed in melanoma and esophageal tumors as compared to their normal tissue counterparts, making the claimed antibodies useful as diagnostic tools, alone or in combination with other diagnostic tools.

Recent Board of Patent Appeals and Interferences Decision

A recent unpublished decision by the Board of Patent Appeals and Interferences, *Ex parte* Goddard, et al. (Appeal 2006-1469, decided April 30, 2007), supports Applicants' arguments that the specification establishes a specific and substantial utility for the PRO3566 polypeptides, and the claimed antibodies. A copy of the decision is attached hereto as Exhibit A.

Although the appealed case involved different facts, including different polypeptides and different data, it is still instructive and similar reasoning in support of utility applies to the instant application.

The claims at issue in the appeal related to isolated polypeptides, including 80% variants of SEQ ID NO:14, as well as the full-length polypeptide of SEQ ID NO:14, with and without its signal peptide. The examiner had argued that microarray DNA data showing differential expression of the nucleic acid in tumor compared to non-tumor tissue were insufficient to establish utility for the claimed subject matter. The examiner in that case made a number of arguments similar to those made in the instant case. In particular, as quoted by the Board on page 5 of its decision, the examiner in that case argued:

> There is no sufficient information or experimental data presented on whether the polypeptide or the nucleic acid of the present invention can serve as a reliable diagnostic marker for colon, lung or prostate tumors; there is no statistical analysis of the expression. Moreover, the assay does not establish a causative link between the polypeptide (or nucleic acid) of the present invention and colon, lung or prostate tumors. Without such critical information, one skilled in the art would not be able to use the molecule of the present invention as a diagnostic marker or as a therapeutic target for treatment of colon, lung or prostate tumors without undue experimentation. Accordingly, the results in Table 8 obtained based upon the assay described in Example 30 only serve as the beginning point for further research on the biological functions or physiological significance of the polypeptide of SEQ ID NO:[]14 or the nucleic acid encoding the polypeptide, and does not provide a specific and substantial utility for the present invention.

Ex parte Goddard at 4.

Despite the examiner's arguments in that case, the Board reversed the examiner's rejection, finding that the data presented in Example 30 of that specification were sufficient to establish a specific and substantial utility for the subject polypeptide. According to the Board, the mRNA data demonstrated differential expression in tumor compared to normal tissue so that the polypeptide of SEQ ID NO:14 has a significant and presently available benefit to the public as a tumor marker.

The Board was unimpressed with the examiner's arguments in that case, many of which are similar to those made in the present application by this Examiner. The Board pointed out that the submitted declarations, including those of Polakis, demonstrated a strong correlation between mRNA levels and protein expression, and that the examiner had not presented any evidence specific to the particular PRO polypeptide to refute that correlation. Finally, the Board pointed out that utility does not require a causative link between the polypeptide (or the nucleic acid) and the particular tumor types.

The Board of Patent Appeals and Interferences Decision Supports Applicants' Position

The reasoning of the Board of Patent Appeals can be applied to the facts of the present case. Here, the data from Example 18 showing differential expression of the PRO3566 polypeptide in skin or esophageal tumor tissue compared to normal skin and esophageal tissue demonstrate a presently available benefit to the public for the PRO3566 polypeptides as tumor markers, as well as for the claimed antibodies that bind the polypeptide of SEQ ID NO:64. Also, the very same declaration by Polakis that was persuasive to the Board has been submitted in this application, along with additional declarations by Polakis, Grimaldi and Scott. The Examiner in this case has not submitted any evidence specific to the PRO3566 polypeptides to rebut the declarations.

Also, Applicants again wish to point out that in other applications owned by the same assignee and filed by some of the same applicants, that rely on *data from the exact same disclosure (although different molecules), Example 18*, and in which the Applicants have submitted *substantially the same references* in support of their asserted utility, the PTO has concluded that:

> [b]ased on the totality of evidence of record, **one of skill in the art would find it more likely than not that an increase in message as measured by RT-PCR would be predictive of an increase in protein expression levels,** absent evidence to the contrary. Therefore, the data presented in Example 18, which demonstrates differential expression of nucleic acids encoding PRO1180, also supports a conclusion of differential expression of PRO1180 polypeptide. Therefore, one of ordinary skill in the art would be able to use the PRO1180 polypeptide diagnostically for distinguishing normal kidney and rectal tumor tissues compared to kidney tumor and normal rectal tissue, as asserted by Applicant.

See *Examiners Reasons for Allowance* in pending Application No. 10/063,529. See also *Examiners Reasons for Allowance* in Application No. 10/063,530, No. 10/063,524, No. 10/063,582, and No. 10/063,583, all of which conclude that the data presented in Example 18, which demonstrate differential expression of the nucleic acids encoding certain PRO polypeptides, also support a conclusion of differential expression of the PRO polypeptides, making the PRO polypeptides and the claimed antibodies that bind the PRO polypeptides useful for diagnostic purposes. These are just a few examples from the many cases where the PTO has agreed with Applicants' position as set forth in their co-pending applications and allowed polypeptide and antibody claims.

Applicants therefore request that the Examiner recognize the utility of the claimed invention, based upon application of the reasoning from the Board of Appeals decision as applied to the facts in this case, the data presented in Example 18, the submitted declarations, and the numerous submitted references.

Utility – Conclusion

Applicants remind the Examiner that the evidence supporting utility does not need to be direct evidence, nor does it need to provide an exact correlation between the submitted evidence and the asserted utility. Instead, evidence which is "reasonably" correlated with the asserted utility is sufficient. *See Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q. 2d 1895 (Fed. Cir. 1996) ("a 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' suffices"); *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739 (Fed. Cir. 1985) (same); *Nelson v. Bowler*, 626 F.2d 853, 857, 206 U.S.P.Q. 881 (C.C.P.A. 1980) (same). In addition, utility need only be shown to be "more likely than not true," not to a statistical certainty. *M.P.E.P.* at § 2107.02, part VII (2004). Considering the evidence as a

whole in light of the relevant standards for establishing utility, Applicants have established at least one specific, substantial, and credible utility. In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the utility rejection under 35 U.S.C. §101.

Rejections under 35 U.S.C. § 112, first paragraph – Enablement

The Examiner also has maintained the rejection of pending Claims 1-5 under 35 U.S.C. § 112, first paragraph. Specifically, the PTO asserts that because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention. *Office Action* at 25. The Examiner argues that Applicant has not provided evidence to demonstrate that the PRO3566 polypeptide and the claimed antibodies have a specific and substantial asserted utility or a well established utility so that one skilled in the art would know how to use the claimed invention. *Office Action* at 25-26.

Applicants submit that in the discussion of the 35 U.S.C. § 101 rejection above, Applicants have established a substantial, specific, and credible utility for the PRO3566 polypeptide and the claimed antibodies. To the extent that the enablement rejection is based on a lack of utility, Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection under 35 U.S.C. §112.

CONCLUSION

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 18, 2007

By: _____

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EXHIBIT A

The opinion in support of the decision being entered today was *not* written for publication and is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte AUDREY GODDARD, PAUL J. GODOWSKI,
AUSTIN L. GURNEY, VICTORIA SMITH, and WILLIAM I. WOOD

Appeal 2006-1469
Application 10/123,212
Technology Center 1600

Decided: April 30, 2007

Before TONI R. SCHEINER, ERIC GRIMES, and LORA M. GREEN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 72-79 and 82-84. We have jurisdiction under 35 U.S.C. § 6(b). Claims 72 and 77 are representative of the claims on appeal, and read as follows:

72. An isolated polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:14;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:14, lacking its associated signal peptide; or

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203577,

wherein the nucleic acid encoding said polypeptide is overexpressed in colon, lung or prostate tumor cells.

77. An isolated polypeptide comprising:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:14;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:14, lacking its associated signal peptide; or

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203577.

Claims 72-79 and 82-84 stand rejected under 35 U.S.C. § 101 as not being supported by either a specific and substantial utility or a well-established utility. Claims 72-76, 83, and 84 stand rejected under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification, and claims 72-76, 83, and 84 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description. Finally, 72-74, 83, and 84 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Young,[1] and claims 72-75, 83, and 84 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Stanton.[2]

We Affirm-In-Part.

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[1] Young, US Patent No. 6,525,174 B1, issued February 25, 2003.
[2] Stanton, US Pub. No. 2002/0110804 A1, published August 15, 2002.

UTILITY

ISSUE

The Examiner contends that the Specification fails to establish a specific and substantial utility or a well-established utility of the polypeptide of SEQ ID NO:14.

Appellants contend that Example 30 presents microarray data demonstrating that the polypeptide of SEQ ID NO:14 is a diagnostic marker for colon, lung, and prostate tumors.

The issue is thus whether the microarray data presented in Example 30 of the Specification is sufficient to establish a specific and substantial utility or a well-established utility for the polypeptide of SEQ ID NO:14?

FACTS

The Examiner rejected claims 72-79 and 82-84 under 35 U.S.C. § 101 as not being supported by either a specific and substantial asserted utility or a well-established utility (Answer 4).

The Examiner notes that the Specification discloses the polypeptide of SEQ ID NO:14 (PRO1866), the nucleic acid sequence encoding it (SEQ ID NO:13), as well as antibodies against the polypeptide. (*Id.*)

As to a well-established utility, the Examiner asserts that the prior art does not demonstrate that the polypeptide of SEQ ID NO:14, the nucleic acid encoding the polypeptide or an antibody that binds to the polypeptide, has "any well-established biological functions or any physiological significance." (*Id.* at 4-5.)

Next, as to a specific and substantial utility, the Examiner references Table 8 of the Specification, which states that the polypeptide is

significantly overexpressed in colon, lung, or prostate tumors compared to a non-cancerous human tissue control. (*Id.* at 5.) The Examiner also notes that the statement is based on a microarray analysis, which measures mRNA levels, and not overexpression of the polypeptide of SEQ ID NO:14 itself. (*Id.*) According to the Examiner:

> There is no sufficient information or experimental data presented on whether the polypeptide or the nucleic acid of the present invention can serve as a reliable diagnostic marker for colon, lung or prostate tumors; there is no statistical analysis of the expression data. Moreover, the assay does not establish a causative link between the polypeptide (or nucleic acid) of the present invention and colon, lung or prostate tumors. Without such critical information, one skilled in the art would not be able to use the molecule of the present invention as a diagnostic marker or as a therapeutic target for treatment of colon, lung or prostate tumors without undue experimentation. Accordingly, the results in Table 8 obtained based upon the assay described in Example 30 only serve as the beginning point for further research on the biological functions or physiological significance of the polypeptide of SEQ ID NO:[]14 or the nucleic acid encoding the polypeptide, and does not provide a specific and substantial utility for the present invention.

(*Id.* at 5-6.)

Appellants argue that patentable utility is demonstrated by Example 30 of the Specification (Br. 4). According to Appellants, Example 30 demonstrates that the gene encoding the polypeptide of PRO1866 (SEQ ID NO:14) "showed significant overexpression in colon, lung, and prostate tumors as compared to a universal normal control," demonstrating "'that the PRO polypeptides of the present invention are useful . . . as diagnostic markers for the presence of one or more cancerous tumors . . . .'" (*Id.*)

Appellants argue further that it is legally incorrect for the Examiner to require specific data, statistical analysis, and further details before accepting the utility set forth in the Specification, as the law is clear that the Examiner must accept Appellants' assertion of utility if that assertion would be credible to one of ordinary skill. (*Id.* at 4-5.)

Appellants assert that the Examiner has used an improper standard in asserting that mRNA levels do not necessarily correlate with the protein level and that protein levels cannot be accurately predicted from mRNA levels. (*Id.* at 6.) The evidentiary standard to be used during examination is preponderance of the evidence under the totality of the circumstances, and thus, Appellants argue, the Examiner "must establish that it is *more likely than not* that one of ordinary skill in the art would doubt the truth of the statement of utility," which "is a much lower standard than a 'necessary' correlation or 'accurate' prediction, and is clearly met for the invention claim." (*Id.* (emphasis in original)).

Moreover, Appellants rely on the Declaration of Dr. Paul Polakis, which states that "*in general, there is a correlation between mRNA levels and polypeptide levels.*" (Br. 6 (emphasis in original)). Appellants also rely on the Declaration of Dr. Victoria Smith, which states that "*microarray analyses actually performed in my laboratory* have shown that when molecules are identified as being overexpressed in a human tumor sample of epithelial origin relative to the 'universal normal control'[3] sample, *in a majority of cases*, that molecule is also confirmed as being overexpressed in

[3] The "universal" epithelial control sample is prepared by pooling non-cancerous human tissues of epithelial origin, including liver, kidney, and lung (Br. 12).

the human tumor tissue sample relative to its human tissue counterpart" (Br. 6 (emphasis in original)). Appellants aver that the two declarations support the assertion of utility in the Specification, *i.e.*, that the PRO1866 polypeptide (SEQ ID NO:14) "is reasonably expected to be overexpressed in colon, lung and prostate tumors and can be used as a cancer diagnostic marker." (*Id.* at 6-7.)

The Specification is drawn to the identification and isolation of novel DNA and to the recombinant production of polypeptides (Specification 1).

Example 30 on page 134 of the Specification is drawn to microarray analysis to detect PRO polypeptides in cancerous tumors.

According to the Specification:

> In the present example, cancerous tumors derived from various human tissues were studied for PRO polypeptide-encoding gene expression relative to non-cancerous human tissue in an attempt to identify those PRO polypeptides which are overexpressed in cancerous tumors. Two sets of experimental data were generated. In one set, cancerous human colon tumor tissue and matched non-cancerous human colon tumor tissue from the same patient ("matched colon control") were obtained and analyzed for PRO polypeptide expression using . . . microarray technology. In the second set of data, cancerous human tumor tissue from any of a variety of different human tumors was obtained and compared to a "universal" epithelial control sample which was prepared by pooling non-cancerous human tissues of epithelial origin, including liver, kidney, and lung. mRNA isolated from the pooled tissues represents a mixture of expressed gene products from these different tissues. Microarray hybridization experiments using the pooled control samples generated a linear plot in a 2-color analysis. The slope of the line generated in a 2-color analysis was then used to normalize the ratios of (test:control detection) within each experiment. The normalized ratios from various experiments were then compared and used to identify clustering

> of gene expression. Thus, the pooled "universal control" sample not only allowed effective relative gene expression determinations in a simple 2-sample comparison, it also allowed multi-sample comparisons across several experiments.
>
> In the present experiments, nucleic acid probes derived from the herein described PRO polypeptide-encoding nucleic acid sequences were used in the creation of the microarray and RNA from the tumor tissues listed above were used for the hybridization thereto. A value based upon the normalized ratio:experimental ratio was designated as a "cutoff ratio". Only values that were above this cutoff ratio were determined to be significant. Table 8 below shows the results of these experiments, demonstrating that various PRO polypeptides of the present invention are significantly overexpressed in various human tumor tissues as compared to a non-cancerous human tissue control. As described above, these data demonstrate that the PRO polypeptides of the present invention are useful not only as diagnostic markers for the presence of one or more cancerous tumors, but also serve as therapeutic targets for the treatment of those tumors.

(*Id.* at 134-35.)

As to PRO1866, the Specification presents Table 8, which states that PRO1866 is overexpressed in colon tumor, prostate tumor, and lung tumor, as compared to universal normal control. (*Id.* at 135.)

The Declaration of Dr. Paul Polakis, dated September 9, 2005, states in paragraphs 4 and 5 that, based on experience with other gene transcripts that are present in human tumor cells at significantly higher levels than in corresponding normal human cells, it has been observed "that there is a strong correlation between changes in the level of mRNA present in any particular cell type and the level of protein expressed from that mRNA in that cell type. In approximately 80% of our observations we have found that increases in the level of a particular mRNA correlates with changes in the

level of protein expressed from that mRNA when human tumor cells are compared with their corresponding normal cells."

The Declaration of Dr. Victoria Smith at paragraph 5, dated September 9, 2005, states that the comparison of mRNA expression levels in human tumor tissues to mRNA expression levels in a sample prepared by pooling non-cancerous human tissues of epithelial origin "is extremely informative and provides a strong basis for the diagnostic determination of cancer in humans."

PRINCIPLES OF LAW

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. *See In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.").

The Court of Appeals for the Federal Circuit addressed the utility requirement in *In re Fisher*, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The *Fisher* court interpreted *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility." 421 F.3d at 1370, 76 USPQ2d at 1229. The *Fisher* court held that § 101 requires a utility that is both substantial and specific. *Id.* at 1371, 76 USPQ2d at 1229. The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to

satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." *Id.*, 76 USPQ2d at 1230.

The court held that a specific utility is "a use which is not so vague as to be meaningless." *Id.* In other words, "in addition to providing a 'substantial' utility, an asserted use must show that that the claimed invention can be used to provide a well-defined and particular benefit to the public." *Id.*

ANALYSIS

We find that the microarray data presented in Example 30 of the Specification is sufficient to establish a specific and substantial utility for the polypeptide of SEQ ID NO:14, and the rejection is reversed.

The microarray data demonstrates that mRNA for the PRO1866 polypeptide (SEQ ID NO:14) is overexpressed in colon tumor, prostate tumor, and lung tumor, as compared to universal normal control. Thus, the polypeptide of SEQ ID NO:14 has a significant and presently available benefit to the public as a tumor marker.

We have considered the Examiner's assertions that microarray analysis measures mRNA levels, and not overexpression of the polypeptide of SEQ ID NO:14 itself. As demonstrated by the Polakis and Smith Declarations, however, there is a strong correlation between mRNA levels and protein expression, and the Examiner has not presented any evidence specific to the PRO1866 polypeptide to refute that.

Finally, the use of the PRO1866 polypeptide as a cancer marker is sufficient to demonstrate utility, and there is no requirement that a causative

link between the polypeptide (or nucleic acid) of the present invention and colon, lung or prostate tumors be demonstrated.

ENABLEMENT

ISSUE

The Examiner contends that the disclosure does not enable one skilled in the art to practice the full genus of peptides encompassed by Appellants' claims.

Appellants contend that one skilled in the art could practice the full scope of the claimed invention, as the skilled artisan has a sufficiently high level of technical competence to identify sequences with at least 80% identity to SEQ ID NO:14, and the specification provides ample guidance such that one of skill in the art could readily test the nucleic acid encoding a variant polypeptide to determine whether it is overexpressed in colon, lung or prostate tumors by the methods set forth in Example 30.

Thus, the issue is does the Specification enable one skilled in the art to use the full scope of the PRO1866 (SEQ ID NO:14) variants of claim 72 without an undue amount of experimentation?

FACTS

The Examiner rejected claims 72-76, 83, and 84 under 35 U.S.C. § 112, first paragraph, on the grounds that the instant disclosure does not enable the full scope of the claimed subject matter (Answer 7).[4]

As we find that Appellants do not argue the claims separately, we focus our attention on independent claim 72. 37 C.F.R. § 41.37(c)(1)(vii) (2006).

The Examiner made the following findings with respect to the factors set out in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).[5]

The breadth of the claims: The Examiner notes that the claims are broad and encompass a genus of variants of SEQ ID NO:14 (Answer 8).

Nature of the invention and the state of the prior art: The Examiner notes that while the Specification teaches that the polypeptide of SEQ ID NO:14 is overexpressed in colon, lung or prostate tumors, the polypeptide "does not have any defined biological functions or activities." (*Id.*)

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[4] The Examiner also rejected claims 72-79 and 82-84 under 35 U.S.C. § 112, first paragraph, on the grounds that "since the claimed invention is not supported by either a specific and substantial utility or a well established utility . . ., one skilled in the art clearly would not know how to use the claimed invention" (Answer 7). Since that rejection relies on the utility rejection, and as we have reversed that rejection, this rejection is also reversed.

[5] The factual considerations discussed in *Wands* are: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Examiner notes further that two variants of the polypeptide of SEQ ID NO: 14 are taught in the prior art by Young (a variant having 92.5% homology) and Stanton (a variant having 96.7% identity), but does not teach that the variants are overexpressed in colon, lung, or prostate tumor cells (Answer 8-9). The Examiner also asserts, citing Haynes,[6] that even if the amount of nucleic acid expressed from SEQ ID NO:13 was overexpressed in colon, lung, or prostate tumor cells, it does not necessarily follow that the polypeptide of SEQ ID NO:14 would also be overexpressed.

The amount of direction or guidance presented and the existence of working examples: The Examiner states that, other than for the polypeptide of SEQ ID NO:14, the Specification fails to provide sufficient direction and/or working examples to make those variants that have the same functions as SEQ ID NO:14, and that there are no examples of functional variants of SEQ ID NO:14 (Answer 9). The Examiner notes further that the Specification does not teach which residues are critical to activity, and thus which modifications will results in a variant having the same function as that of SEQ ID NO:14. (*Id.* at 9-10.)

The relative skill of those in the art, the predictability or unpredictability of the art, and the quantity of experimentation necessary: While acknowledging that the level of skill in the art of DNA recombination technology is relatively high, the Examiner states that procedures for making

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[6] Haynes et al. (Haynes), "Proteome analysis: Biological assay or data archive," *Electrophoresis*, Vol. 19, pp. 1862-1871 (1998). The Examiner cites Haynes for the proposition that "[t]he prior art teaches that the multi-level control of protein synthesis and degradation in cells means that only the direct analysis of mature protein products can reveal their correct identities, their relevant state of modification and/or association and their amounts" (Answer 9).

variants of the polypeptide of SEQ ID No: 14 as set forth by the claims that still retain its activity are not conventional and are unpredictable. (*Id.* at 10.) The Examiner concludes that "due to lack of the disclosure of the functions of encompassed polypeptides structurally related to SEQ ID NO:14, [lack of] sufficient guidance and/or working examples provided in the specification, and [lack of] teachings in the art on how to use those variants of the polypeptide of SEQ ID NO:14, it would take undue experimentation for one skilled in the art to make and use the variants of polypeptide of SEQ ID NO:14." (*Id.* at 10-11.)

Appellants argue that "the claimed variants all share the functional limitation that '*the nucleic acid encoding said polypeptide is overexpressed in colon, lung or prostate tumor cells*," and that Example 30 of the Specification provides step-by-step guidelines and protocols for the microarray analysis (Br. 28 (emphasis in original)). Appellants assert further that "[t]he specification provides detailed guidance as to changes that may be made to a PRO polypeptide without adversely affecting its activity (page 81, line 17, to page 83, line 26)" (Br. 29).

Appellants submit

> that the specification provides ample guidance such that one of skill in the art could readily test the nucleic acid encoding a variant polypeptide to determine whether it is overexpressed in colon, lung or prostate tumors by the methods set forth in Example 30. Furthermore, one of ordinary skill in the art has a sufficiently high level of technical competence to identify sequences with at least 80% identity to SEQ ID NO:14. Accordingly, one of ordinary skill could practice the claimed invention without undue experimentation.
>
> The claims currently recite polypeptide sequences associated with a specific biological activity of the encoding nucleic acid. This biological activity together with the well

> defined relatively high degree of sequence identity and general knowledge in the art at the time the invention was made, sufficiently defines the claimed genus such that, one skilled in the art, at the effective date of the present application, would have known how to make and use the claimed polypeptide sequences without undue experimentation.

(*Id.*)

As noted with respect to the utility rejection, Table 8 of the Specification states that PRO1886 is overexpressed in colon tumor, prostate tumor, and lung tumor, as compared to universal normal control. (Specification 135.)

Page 81, line 17 to page 83, line 26 of the Specification provides general guidance as to the generation of PRO polypeptide variants, which guidance is applicable to the generation of any polypeptide variant. The Specification does not disclose any guidance that is specific to the PRO1866 (SEQ ID NO:14) polypeptide. The Specification also does not present any data as to the biological function of PRO1866 other than the microarray data that demonstrates that it may be used as a tumor marker.

PRINCIPLES OF LAW

Enablement is a question of law, based on underlying findings of fact. *See, e.g., In re Wands*, 858 F.2d 731, 735, 8 USPQ2d 1400, 1402 (Fed. Cir. 1988). "When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the

invention provided in the specification of the application." *In re Wright*, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

"[T]o be enabling, the specification . . . must teach those skilled in the art how to make and use *the full scope of the claimed invention* without 'undue experimentation.'" *Wright*, 999 F.2d at 1561, 27 USPQ2d at 1513 (emphasis added), *quoted in Genentech, Inc. v. Novo Nordisk, A/S,* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997). Thus, "there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 & n. 23, 20 USPQ2d 1438, 1445 & n. 23 (Fed. Cir. 1991), *quoted in Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1372, 52 USPQ2d 1129, 1138 (Fed. Cir. 1999).

"Patent protection is granted in return for an enabling disclosure . . . , not for vague intimations of general ideas that may or may not be workable." *Genentech*, 108 F.3d at 1365, 42 USPQ2d at 1005. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, *reasonable detail* must be provided in order to enable members of the public [skilled in the art] to understand and carry out the invention." *Id.* at 1366, 42 USPQ2d at 1005 (emphasis added).

ANALYSIS

While Appellants have demonstrated that the polypeptide of SEQ ID NO:14 is a diagnostic marker for colon, lung, and prostate cancer, the Specification sets forth no biological activity or function for the protein. All

that is disclosed is the sequence information for SEQ ID NO:14. Moreover, the Specification does not disclose which portions of the polypeptide of SEQ ID NO:14 are required for activity, and which regions are tolerant to substitution. With respect to the variants, all that is disclosed by the Specification are methods of making polypeptide variants in general, and information as to what amino acid substitutions are generally considered by the skilled artisan to be conservative. The Specification, however, does not disclose any guidance of generating variants of the polypeptide of SEQ ID NO:14 that is specific to SEQ ID NO:14, wherein the variant is overexpressed in colon, lung, or prostate tumor cells.

Without information as to the biological activity or function, it would be unpredictable to the skilled artisan which variants of SEQ ID NO:14 would also perform as a diagnostic marker for colon, lung, and prostate cancer. Claim 72 is drawn to variants having 80% amino acid sequence identity, but, as noted by the Examiner, two variants of the polypeptide of SEQ ID NO:14 having higher sequence identity have been disclosed by Young (a variant having 92.5% homology) and by Stanton (a variant having 96.7% identity), but have not been shown to be overexpressed in colon, lung, or prostate tumor cells.

Given the lack of guidance as to the biological function or activity of the polypeptide of SEQ ID NO:14, and the lack of guidance as to those variants of SEQ ID NO:14 that would be expected to also perform as a diagnostic marker for colon, lung, and prostate cancer, as well as the enormous number of variants that would have 80% sequence identity with

SEQ ID NO:14,[7] it would require an undue amount of experimentation by one skilled in the art to use the full scope of variants encompassed by claim 72 without further guidance from Appellants.

CONCLUSIONS OF LAW

We conclude that the Specification does not enable one skilled in the art to use the full scope of the PRO1866 (SEQ ID NO:14) variants of claim 72 without an undue amount of experimentation, and the rejection is affirmed.

WRITTEN DESCRIPTION

ISSUE

The Examiner contends that the claims are drawn to an isolated polypeptide having 80%, 85%, 90%, 95%, and 99% sequence identity to SEQ ID NO:14, and due to the breadth of the claimed genus and the lack of definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the Appellants were in possession of the claimed genus

Appellants contend that the genus of polypeptides with at least 80% sequence identity to SEQ ID NO:14, which possess the functional property of having a nucleic acid which is overexpressed in colon, lung or prostate tumors, would meet the requirement of 35 U.S.C. § 112, first paragraph, as providing adequate written description.

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[7] The polypeptide of SEQ ID NO:14 is 541 amino acids long, and as there are 20 naturally occurring peptides, the number of variants that would have 80% sequence identity to SEQ ID NO:14 would be enormous.

Thus, the issue is does the disclosure as filed provide adequate written description to support the genus of variants of the polypeptide of SEQ ID NO:14 encompassed by claim 72?

FACTS

The Examiner rejected claims 72-76, 83, and 84 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention (Answer 11).

As we find that Appellants do not argue the claims separately, we focus our attention on independent claim 72. 37 C.F.R. § 41.37(c)(1)(vii) (2006).

The Examiner notes that the claims are drawn to an isolated polypeptide having 80%, 85%, 90%, 95%, and 99% sequence identity to SEQ ID NO:14, asserting that the claims do not require that the polypeptide have any particular conserved structure or any other distinguishing feature. (Answer 12.) According to the Examiner,

> [w]hile the claims recite a limitation "wherein the nucleic acid encoding said polypeptide is overexpressed in colon, lung or prostate tumor cells," such a limitation does not limit the scope of the invention in actuality because the specification does not reasonably identify or confirm that the polypeptide or the nucleic acid encoding the polypeptide is overexpressed in colon, lung or prostate tumor cells. Thus, the claims are drawn to a genus of polypeptides that is defined only by a partial structure in the form of a recitation of percent identity.

(*Id.*)

Moreover, according to the Examiner, the disclosure of SEQ ID NO:14 and its encoding nucleic acid sequence, SEQ ID NO:13, "does not adequately support the scope of the claimed genus, which encompasses a substantial variety of homologues or variants of the polypeptide of SEQ ID NO:14." (*Id.*) The disclosure as filed, the Examiner asserts, fails to provide sufficient description as to structural and functional features of the claimed genus, such as conserved regions that are critical to the structure and function of the genus claimed. (*Id.* at 13.) Thus, "[t]here is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function." (*Id.*)

The Examiner concludes:

> Due to the breadth of the claimed genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the Appellant was in possession of the claimed genus. Accordingly, only the isolated polypeptide comprising SEQ ID NO:14 . . ., but not the full breadth of the claims meets the written description provision of 35 U.S.C. § 112, first paragraph.

(*Id.* at 13-14.)

Appellants assert that "the genus of polypeptides with at least 80% sequence identity to SEQ ID NO:14, which possess the functional property of having a nucleic acid which is overexpressed in colon, lung or prostate tumors would meet the requirement of 35 U.S.C. § 112, first paragraph, as providing adequate written description." (Br. 32.) According to Appellants, the level of skill in the art of recombinant DNA technology is high, and thus "the teachings imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made." (*Id.*)

Appellants argue further that Example 30 provides step-by-step guidelines and protocols for performing the microarray analysis, thus the skilled artisan could test variants of the PRO1866 polypeptide (SEQ ID NO:14) to determine if they are overexpressed in colon, lung, or prostate tumor cells. (*Id.*) Moreover, Appellants aver, the Specification (page 81, line 17, to page 83, line 26) provides detailed guidance as to what changes may be made to the PRO polypeptide without affecting its activity, such as exemplary and preferred amino acid substitutions (Br. 33). "Accordingly," Appellants assert, "one of skill in the art could identify whether a variant PRO1866 sequence falls within the parameters of the claimed invention." (*Id.*).

Appellants note that factors to be considered in evidencing possession of a claimed genus include structural features and functional activity, which they assert they have provided by reciting a structural feature—80% sequence identity to SEQ ID NO:14—as well as a specific functional activity for the encoding nucleic acids. (*Id.*)

As noted above with respect to the enablement rejection, page 81, line 17 to page 83, line 26 of the Specification provides general guidance as to the generation of PRO polypeptide variants. The Specification does not disclose any guidance that is specific to the PRO1866 (SEQ ID NO:14) polypeptide. The Specification also does not present any data as to the biological function of PRO1866 other than the microarray data that demonstrates that it may be used as a tumor marker.

PRINCIPLES OF LAW

The requirement for written description under the first paragraph of section 112 is separate and distinct from the enablement requirement of that paragraph. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991). Compliance with the written description requirement is a question of fact. *Id.*

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997 (bracketed material in original). The claims in *Lilly* were directed generically to vertebrate or mammalian insulin cDNAs. *See id.* at 1567, 43 USPQ2d at 1405. The court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs.

The *Lilly* court explained that

> a generic statement such as. . . 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. at 1568, 43 USPQ2d at 1406. Finally, the *Lilly* court set out exemplary ways in which a genus of cDNAs could be described:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by

> nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. at 1569.

Our appellate reviewing court revisited the issue of describing DNA. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The *Enzo* court held that a claimed DNA could be described without, necessarily, disclosing its structure. The court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" *See id.* at 1324, 63 USPQ2d at 1613 (emphasis omitted, ellipsis and bracketed material in original).

Our appellate review court has also noted that "*Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

This standard applies to polypeptides as well as DNAs. *See University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 925, 69 USPQ2d 1886, `893 (Fed. Cir. 2004): "We agree with Rochester that *Fiers*,

Lilly, and *Enzo* differ from this case in that they all related to genetic material whereas this case does not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue."

With respect to the use of an assay to support written description, in *University of Rochester*, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human." *Id.* at 918, 69 USPQ2d at 1888. The patent "described in detail how to make cells that express either COX-1 or COX-2, but not both . . . , as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[']" *Id.* at 927, 69 USPQ2d at 1895.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of *which* peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims failed to meet the description requirement of § 112. *See id.* ("As pointed out by the district court, the '850 patent does not disclose just 'which "peptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting PGHS-2.' . . . Without such disclosure, the claimed methods cannot be said to have been described.").

ANALYSIS

We find that the disclosure as filed does not provide adequate written description to support the genus of variants of the polypeptide of SEQ ID NO:14 encompassed by claim 72, and the rejection is affirmed.

Claim 72 is drawn to variants that have 80% sequence identity to SEQ ID NO:14, wherein the nucleic acid encoding said polypeptide is overexpressed in colon, lung or prostate tumor cells. The Specification does not disclose a biological function or activity of the polypeptide of SEQ ID NO:14, and also does not disclose a single variant that also performs as a diagnostic marker for colon, lung, and prostate cancer. Thus, the genus encompasses an enormous number of sequences, but the Specification only describes a single member of that genus—SEQ ID NO:14.

In addition, there is no disclosure of sufficiently detailed, relevant identifying characteristics, such as other physical and/or chemical properties, or functional characteristics, that when coupled with a known or disclosed correlation between function and structure (i.e., the sequence), or some combination of such characteristics, would constitute an adequate written description of the claimed invention. All that is disclosed is the amino acid sequence and that it may be used as a diagnostic marker for certain tumor types. While the skilled artisan may be able to determine polypeptides that have 80% sequence identity with SEQ ID NO:14, without any disclosure of function or what residues are required for the polypeptide to function as a diagnostic marker, the skilled artisan cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus that would be useful as a diagnostic marker.

Moreover, just as in the *University of Rochester* case, discussed above, the present application discloses a broad genus of chemical compounds (polypeptides having 80% sequence identity to SEQ ID NO:14) but the claims are limited to only those compounds having a desired characteristic (wherein the nucleic acid encoding said polypeptide is overexpressed in colon, lung, or prostate tumor cells). Just as in *University of Rochester*, the present specification does not disclose which nucleic acids encoding the many possible polypeptides having 80% sequence identity to SEQ ID NO:14 are overexpressed in colon, lung, or prostate tumor cells.

Granted, those skilled in the art could screen libraries of naturally occurring DNAs for overexpression in colon, lung or prostate tumor cells to identify for themselves specific DNAs that encode polypeptides having 80% sequence identity to SEQ ID NO:14. That, however, does not make up for the deficiency of the specification's description. The *University of Rochester* court specifically noted that the patent at issue there disclosed screening assays to identify compounds having the desired characteristic, but nonetheless held that the description was inadequate. The same holds true here.

PRIOR ART

ISSUE

The Examiner contends that claims 72-74, 83, and 84 are anticipated by Young, and that claims 72-75, 83, and 84 are anticipated by Stanton.

Appellants contend that have demonstrated invention prior to the effective filing dates of Young and Stanton, and thus Young and Stanton are not anticipatory art within the meaning of 35 U.S.C. § 102(e).

Thus, the issue is whether the Declaration submitted under 37 C.F.R. § 1.131 is sufficient to overcome the rejections over the prior art made under 35 U.S.C. § 102(e)?

FACTS

The Examiner rejected claims 72-74, 83, and 84 under 35 U.S.C. § 102(e) as being anticipated by Young (Answer 14).

According to the Examiner, Young teaches a polypeptide that shares 92.5% sequence identity with SEQ ID NO:14. (*Id.*)

The Examiner rejected claims 72-75, 83, and 84 under 35 U.S.C. § 102(e) as being anticipated by Stanton. (*Id.* at 15.)

According to the Examiner, Stanton teaches a polypeptide that shares 96.7% sequence identity with SEQ ID NO: 14. (*Id.*)

Appellants do not argue the merits of the rejections. Rather, Appellants assert that the declaration submitted under 37 C.F.R. § 1.131 is sufficient to show invention prior to the effective filing dates of Young and Stanton (Br. 34).

Appellants cite the 37 C.F.R. § 1.131 Declaration of Dr. Goddard, Dr. Godawski, Dr. Gurney, Dr. Smith, and Dr. Wood, to support the proposition that the inventors "conceived and reduced to practice the PRO1866 polypeptide and its encoding nucleic acid sequence in the United States prior to December 4, 1998." (*Id.* (emphasis removed).) According to Appellants, "the Declaration clearly establishes that the claimed polypeptides and the nucleic acids encoding them, were conceived and reduced to practice prior to December 4, 1998, and that the differential expression of PRO1866 in the

multiple types of cancer cells based on microarray analysis were demonstrated prior to March 31, 2000." (*Id.* at 35.)

Appellants cite MPEP § 715.03 for the proposition that:

> proof of prior completion of a species different from the reference species will be sufficient to overcome a reference indirectly under 37 C.F.R. § 1.131 if the reference species would have been obvious in view of the species shown to have been made by applicants. Alternatively, *the applicant may be able to antedate the reference indirectly by demonstrating possession of the claimed genus prior to the reference date.* The test is whether the species completed by applicant prior to the reference date provided an adequate basis for inferring that the invention has generic applicability. . . . The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the applicant possessed so much of the invention as is shown in the reference. *In re Schaub*, 537 F.2d 509, 190 U.S.P.Q. 324 (C.C.P.A. 1976).

(Br. at 35-36 (footnote omitted) (emphasis in original)).

Appellants cite their arguments regarding the written description rejection, asserting that the "disclosed polypeptide of SEQ ID NO[:]14 is *representative for a genus encompassing its variants.*" (*Id.* at 36.)

Appellants also cite Example 14 of the Synopsis of Application of Written Description Guidelines issued by the USPTO, which Appellants note states

> that protein variants meet the requirements of 35 U.S.C. § 112, first paragraph, as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins are routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the variant proteins possess the

> specified functional activity and at least 95% sequence identity to the reference sequence.

(Br. 36.)

The Declaration submitted under 37 C.F.R. § 1.131 of Dr. Audrey Goddard, Dr. Paul J. Godowski, DR. Austin Gurney, Dr. Victoria Smith, and Dr. William I. Wood, dated October 26, 2004, states at ¶10 that "[b]oth the DNA-44174 and the PRO1866 polypeptide sequences were obtained prior to December 4, 1998." It further states at ¶17 that "the microarray analysis of mRNA expression of PRO1866 in cancer cells was conducted prior to March 31, 2000, and the data indicate that the mRNA of PRO1866 is overexpressed in colon, lung, and prostate tumors."

PRINCIPLES OF LAW

A declaration under 37 C.F.R. § 1.131 must establish possession of either the whole invention claimed or of something falling within the claim such as a species of a claimed genus, such that the claim as a whole reads on it. *See In re Tanczyn*, 347 F.2d 830, 831-32, 146 USPQ 298, 300 (CCPA 1965); *see also* MPEP § 715.02

Where the disclosure in the prior art is only a single species of a genus claim, appellant can overcome the rejection through the use of a 131 declaration by showing prior possession of the species disclosed in the reference. *In re Stempel*, 241 F.2d 755, 759, 113 USPQ 77, 81 (CCPA 1957). If the species disclosed in the reference is different from the species that was disclosed in the 131 declaration, the 131 declaration can only overcome the reference if the species shown in the reference would have been obvious in view of the species shown to have been made by appellant.

See In re Clarke, 356 F.2d 987, 961, 148 USPQ 665, 668-69 (CCPA 1966). If appellant cannot show possession of the species of the reference, appellant may be able to antedate the reference by showing prior completion of one or more species such that appellant was in possession of the claimed genus. *See id.* Note it is not necessary that the evidence demonstrate that appellant viewed the invention as encompassing more than the species actually made, only that the evidence would persuade one skilled in the art that appellant possessed so much of the invention as is shown in the reference. *In re Schaub*, 537 F.2d 509, 512 131, 190 USPQ 324, 326 (CCPA 1976). *See also* MPEP 715.03.

ANALYSIS

The species disclosed by the Declaration submitted under 131 is different than that disclosed by either the Young or Stanton reference. In addition, we have already determined in reviewing the rejection under 35 U.S.C. § 112, first paragraph, for written description, that the disclosure of a single species, *i.e.*, the polypeptide of SEQ ID NO:14 does not demonstrate that Appellants had possession of the claimed genus. Thus, we need to determine if the species disclosed by Young and Stanton would be obvious over the polypeptide of SEQ ID NO:14.

Appellants' claim 72 is drawn to a polypeptide having 80% sequence identity to SEQ ID NO:14. Thus, the species of Young and Stanton are clearly encompassed by the claims. Moreover, Appellants disclose that the polypeptide is overexpressed in colon, lung or prostate tumor cells. As we have already found above, however, neither the Declaration nor the disclosure as filed provides guidance as to what regions are necessary for

activity, or what the biological activity is, other than its use as a diagnostic marker. Thus, we conclude that there is nothing in the Declaration or the disclosure as filed that would suggest to one of ordinary skill in the art the species disclosed by Young and Stanton, and thus that the polypeptide of SEQ ID NO:14 does not render obvious the species disclosed by Young and Stanton. *See In re Baird,* 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.").

Thus, as the Declaration submitted under 37 C.F.R. § 1.131 is not sufficient to overcome the rejections over the prior art made under 35 U.S.C. § 102(e), the rejections of claims 72-74, 83, and 84 under 35 U.S.C. § 102(e) as being anticipated by Young, and claims 72-75, 83, and 84 under 35 U.S.C. § 102(e) as being anticipated by Stanton, are affirmed.

CONCLUSION

In summary, we reverse the rejection of claims 72-79 and 82-84 under 35 U.S.C. § 101 as not being supported by either a specific and substantial utility or a well-established utility. We do, however, affirm the rejection of claims 72-76, 83, and 84 under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification; the rejection claims 72-76, 83 and 84 under 35 U.S.C. § 112, first paragraph, as lacking adequate written description; the rejection of claims 72-74, 83 and 84 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Young; and the rejection of claims 72-75, 83 and 84 under 35 U.S.C. § 102(e) as being anticipated by Stanton.

AFFIRMED-IN-PART

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